In re application of: Application No.:

Snyder, E., et al. 09/939,476 08/23/01

Group No.: Not yet assigned Examiner: Not yet assigned

Filed: For:

ENGRAFTABLE NEURAL PROGENITOR AND STEM CELLS FOR BRAIN TUMOR THERAPY

front lobe. Animals were sacrificed on day 12 and 21 (shown); c) 4x C17.2 cells (red) seen actively migrating across central commisure (double immunofluorescence), e) 20x C17.2 cells (blue) seen entering tumor (black arrows) (Xgal/neutral red). (Figs. 4F, 4G) Intraventricular: 5x10⁴ CNS-1 tumor cells were implanted into right frontal lobe. On day 6, 8x10⁴ C17.2 cells were injected into right or left (shown)

lateral ventricle.

On page 12, please replace the heading to the first paragraph, line 12 with the following heading:

B2 BudR labelling of engrafted C17.2 cells:

IN THE CLAIMS:

Please cancel claims 1 - 15.

Please add claims 16 - 22 as follows:

- A method for treating a tumor mass present within a living host subject, said method 16. comprising the steps of obtaining a plurality of genetically modified mammalian neural stem cells comprising a primordial neural stem cell of mammalian origin which:
 - remains uncommitted and undifferentiated prior to in-vivo implantation as a (i) mitotic, self-renewing cell,
 - (ii) is implantable in-vivo into the central nervous system of the host subject as an uncommitted cell,
 - (iii) migrates from the site of implantation to a location where there is at least one tumor mass comprising tumor cells within the host subject,
 - can collect and accumulate within the tumor mass in-situ, (iv)
 - comprises mammalian neural stem cell genomic DNA which is genetically (v) modified to include exogenous genetic material coding for a specific protein product which is expressed by said modified neural stem cells to treat the tumor cells as may be present at said first location in-situ;

implanting such genetically modified neural stem cells in-vivo within the living host subject;

allowing said implanted genetically modified neural stem cells to migrate to a location where the tumor mass is present and to collect around and to accumulate within the tumor mass at said location; and



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allowing said genetically modified neural stem cells which have collected around and accumulated within the tumor mass at said location within the host subject to express at least one exogenous protein product in-situ as a treatment.

- 17. The method of claim 16, wherein the tumor mass is within the central nervous system of the host subject.
- 18. The method of claim 17, wherein the tumor mass is a malignant glioma.
- 19. The method of claim 16, wherein said cell has been modified with exogenous genetic material encoding at least one viral vector and a heterologous gene to be expressed subsequently for the making and releasing of viral particles and transfection of tumor cells.
- 20. The method of claim 16, wherein said cell has been modified with exogenous genetic material encoding a viral vector comprising a nucleic acid sequence encoding for a product selected from the group consisting of suicide genes, differentiating agents, and receptors for trophins to be incorporated into tumor cells.
- 21. A method of treating a tumor present in the central nervous system of a host comprising, administering to said host murine neural stem cells capable of expressing cytosine deaminase and thereafter administering to said host 5-fluorocytosine, wherein the cytosine deaminase producing cells convert the no-toxic 5-fluorocytosine to toxic 5-fluorocytosine.
- 22. The method of claim 21, wherein the murine neural stem cell is C17.2.